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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,513	05/01/2001	Edward F. Delong	MBA-101	7869

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EXAMINER	
STRZELECKA, TERESA E	
ART UNIT	**PAPER NUMBER**
1637	9

DATE MAILED: 08/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/847,513	DELONG ET AL.	
	Examiner	Art Unit	
	Teresa E Strzelecka	1637	

-- The MAILING DATE of this communicati n appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-129* is/are pending in the application.

4a) Of the above claim(s) *8-36 and 45-129* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 37-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 May 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1-7 and 37-44, SEQ ID NO: 4) in Paper No. 8 is acknowledged. The traversal is on the ground(s) that claims 1 and 2 are generic to the clones claimed in dependent claims 7-36. This is not found persuasive because, as stated in the restriction requirement, the restriction requirement is subject to non-allowance of the linking claims. Therefore, should claims 1 and 2 become allowable, the dependent claims may be rejoined with the linking claims.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 8-36 and 45-129 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

4. Claims 1-7 and 37-44 will be examined.

Deposit of Biological Material

5. The specification lacks complete deposit information for the deposit of cells containing the clone BAC31A8.

Because it is not known whether clones possessing the properties of BAC31A8 are known and publicly available or can be reproducibly constructed based on knowledge of the nucleotide

sequences of these clones and because the best mode disclosed by the specification requires the use of these clones, a suitable deposit for patent purposes is required. Accordingly, filing of evidence of the reproducible production of these clones or cells containing these clones or filing of a deposit commensurate in scope with the claims, is required. Without a publicly available deposit of the clone BAC31A8, one of skill in the art could not be assured of the ability to practice the invention as claimed. Note that the best mode is not satisfied by a written disclosure unless the exact embodiment is reasonably reproducible from that disclosure.

Although the specification acknowledges a deposit of the clone (Applicants provided a declaration that clones BAC31A8, BAC40E8, BAC41B4, BAC64A5 were deposited in ATCC on February 21, 2001), it is not clear whether maintenance and availability requirements have been met. For further information concerning deposit practice, applicants attention is directed to In re Lundark 773 F 2d 1216 227 USPQ 90 CCAFC, M.P.E.P. 608.01 (p) (c), and 37CFR 1.801-1.809.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See C.F.R. 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CRF 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

Drawings

6. The drawings are objected to under 37 CFR 1.83(a) because they fail to show features as described in the specification. Figure 40 shows a picture of two microfuge tubes, one of which contains a cell suspension with a reddish pigmentation, as described on page 26, lines 25 and 26 and page 27, lines 1-3. As the picture is black and white, it is not possible to distinguish the two tubes. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-6 and 37-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species

situations that "Satisfactory disclosure of a ``representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification. The genus includes variants for which no written description is provided in the specification. This large genus is represented in the specification by only the particularly named SEQ ID Nos (4, 8, 10, 12, ...62, 64; 30 sequences total). Thus, applicant has express possession of only 30 sequences of rhodopsin genes, in a genus which comprises of millions of different possibilities. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations is provided. Further, these claims encompass allelic variants including insertions and mutations, and only specific nucleic acid sequences have been provided. No written description of alleles, of upstream or downstream regions containing additional sequence has been provided in the specification.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516,

> 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the proteorhodopsin gene lacks any specific structure, is precisely the situation of naming a type of material which is generally known to likely exist, but, except for the 30 specific sequences, is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim to "a proteorhodopsin gene", for example.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as a proteorhodopsin gene, without any definition of the particular sequences claimed.

In the instant application, certain specific SEQ ID NOs are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which comprise sequences with SEQ ID NO: 4, 8, 10, 12, ...62 and 64. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

8. Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The deposit of cells containing clone BAC31A8 has been noted in this application (see, for example, page 52). While the specification teaches the sequence of a 750 bp insert (i.e. SEQ ID NO: 4) present in clone BAC31A8, the specification does not teach the complete sequence of the BAC vector. Because the sequence of the clone BAC31A8 is not known and because it is not clear whether BAC31A8 is known and publicly available or can be reproducibly isolated from nature without undue experimentation and because the gene product of claim 7 requires the use of clone BAC31A8, a suitable deposit for patent purposes is required. Without the publicly available deposit of the above clone, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed.

To satisfy the requirements for deposit, the specification should be amended to recite that the deposit has been made under the Budapest Treaty and to include the date of the deposit and the address of the depository. For further information concerning deposit practice, Applicants attention is directed to 37 CFR 1.801-1.809 and MPEP2401-2411.05.

Claim interpretation

9. The following interpretations are used for the purpose of art rejections:

A) The term "proteorhodopsin" is not defined in the specification, therefore it is interpreted as referring to any rhodopsin.

B) In claim 39, the phrase "for producing said proteorhodopsin protein in a host" is treated as an intended use of the product, and therefore not taken into account when the claim is compared with the prior art.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1, 2, 5 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Kitajima et al. (Biochem. Biophys. Res. Comm., vol. 220, pp. 341-345, 1996).

Regarding claim 1, Kitajima et al. teach a proteorhodopsin gene comprising an isolated DNA sequence for encoding a proteorhodopsin protein (Kitajima et al. teach genes encoding three rhodopsins: cR-3, chR-3 and csR-3 (Abstract; page 342, paragraphs 6, 7, 8; page 343, paragraphs 1, 2; Fig. 1).)

Regarding claim 2, Kitajima et al. teach that the genes were retrieved from genomic fragments of naturally occurring marine bacteria *Haloarcula vallismortis* (page 341, the last paragraph; page 344, third paragraph).

Regarding claim 5, Kitajima et al. teach retrieval of the genes from a recombinant Sac I library (page 344, paragraph 7).

Regarding claim 37, Kitajima et al. teach amplification by polymerase chain reaction (page 344, third paragraph).

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kitajima et al. in view of Monaco et al. (Trends in Biotech., vol. 12, pp. 280-286, 1994).

A) Claim 6 is drawn to the proteorhodopsin gene of claim 5, wherein the naturally occurring bacterial genomic fragment is retrieved from a bacterial artificial chromosome library.

B) Kitajima et al. teach cloning of rhodopsin gene, but do not teach bacterial artificial chromosome (BAC) library.

C) Monaco et al. teach cloning BACs cloning system in E. coli (Table 1; page 283, third paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used BACs of Monaco et al. to clone bacterial fragments of Kitajima et al. The motivation to do so, provided by Monaco et al., would have been that the BAC clones were stable over many generations and could be transformed into E. coli very efficiently (page 283, third paragraph).

14. Claims 39 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kitajima et al. in view of Shimono et al. (FEBS Letters, vol. 420, pp. 54-56, 1997).

A) Claim 39 is drawn to the proteorhodopsin gene of claim 1, wherein said proteorhodopsin gene is derived from a marine environment and placed in an expression vector for producing said proteorhodopsin protein in a host. Claim 41 is drawn to the proteorhodopsin gene of claim 39, wherein the host is a bacterium.

B) Kitajima et al. teach rhodopsin genes obtained from marine environment, namely, from a marine bacterium *Haloarcula vallismortis* (page 220, the last paragraph). Kitajima et al. do not teach placing the genes in bacterial expression vectors.

C) Shimono et al. teach placing a gene encoding a rhodopsin from *Natronobacterium pharaonis* into an expression vector pET21c for expression in a bacterium host, E. coli (page 54, paragraphs 5 and 6).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have cloned the rhodopsin genes of Kitajima et al. into an expression vector of Shimono et al. The motivation to do so, provided by Shimono et al., would have been that expression of rhodopsin in E. coli allowed investigation of photochemical properties of rhodopsins using site-directed mutagenesis (page 56, the last paragraph).

15. Claim 40 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kitajima et al. in view of Shimono et al. (FEBS Letters, vol. 420, pp. 54-56, 1997), as applied to claim 39 above, and further in view of Zozulya et al. (Protein Eng., vol. 3, pp. 453-458, 1990).

A) Claim 40 is drawn to the proteorhodopsin gene of claim 39, wherein the host is an artificial membrane system.

B) Neither Kitajima et al. nor Shimono et al. teach the host being an artificial membrane system.

C) Zozulya et al. teach expression of rhodopsin in cell-free translation system supplemented with artificial membranes, phosphatidylcholine liposomes (page 453, the last paragraph; page 454, first and second paragraphs).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used artificial membranes of Zozulya et al. for placing a rhodopsin expression vector of Kitajima et al. and Shimono et al. The motivation to do so, as stated by Zozulya et al., would have been that "... The other obvious advantage of preparative cell-free expression system, as compared to the alternative ones, include: experimental simplicity and speed, the possibility of

obtaining easily protein labeled with radioactive or modified amino acids, the possibility of inserting a membrane protein in a desired lipid environment co-translationally and, last but not least, comparatively low price of an experiment." (page 457, the last paragraph).

16. Claim 42 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kitajima et al. in view of Shimono et al. (FEBS Letters, vol. 420, pp. 54-56, 1997), as applied to claims 39 and 41 above, and further in view of Zozulya et al. (Protein Eng., vol. 3, pp. 453-458, 1990).

A) Claim 42 is drawn to the proteorhodopsin gene of claim 41, wherein the host is a cell membrane preparation of a bacterium.

B) Neither Kitajima et al. nor Shimono et al. teach the host being an artificial membrane system.

C) Zozulya et al. teach expression of bovine rhodopsin in cell-free translation system supplemented with artificial membranes, phosphatidylcholine liposomes (page 453, the last paragraph; page 454, first and second paragraphs). Zozulya et al. teach membranes prepared from eukaryotic microsomes of rat brain cortex and dog pancreas (page 454, third paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used membrane preparations of Zozulya et al. for placing a rhodopsin expression vector of Kitajima et al. and Shimono et al. The motivation to do so, as stated by Zozulya et al., would have been that "... The other obvious advantage of preparative cell-free expression system, as compared to the alternative ones, include: experimental simplicity and speed, the possibility of obtaining easily protein labeled with radioactive or modified amino acids, the possibility of inserting a membrane protein in a desired lipid environment co-translationally and, last but not least, comparatively low price of an experiment." (page 457, the last paragraph). Therefore, it

would have been obvious to one of ordinary skill in the art to have used bacterial-derived membranes in a system in which bacterial proteins were expressed.

17. Claim 43 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kitajima et al. in view of Shimono et al. (FEBS Letters, vol. 420, pp. 54-56, 1997), as applied to claim 39 above, and further in view of Mollaaghababa et al. (PNAS, vol. 93, pp. 11482-11486, 1996).

A) Claim 43 is drawn to the proteorhodopsin gene of claim 39, wherein the host is a eukaryote.

B) Neither Kitajima et al. nor Shimono et al. teach placing genes in eukaryotic expression vectors.

C) Mollaaghababa et al. teach expression of bovine rhodopsin in eukaryotic host cells of *Saccharomyces cerevisiae* (Abstract; page 11482, the last paragraph; page 11483, paragraphs 1, 2).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the yeast cells of Mollaaghababa et al. to express rhodopsins of Kitajima et al. The motivation to do so, provided by Mollaaghababa et al., would have been that expression in yest cells provided properly folded and fully functional rhodopsin (Abstract; page 11486, the last paragraph).

18. Claim 44 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kitajima et al. in view of Shimono et al. (FEBS Letters, vol. 420, pp. 54-56, 1997) and Mollaaghababa et al. (PNAS, vol. 93, pp. 11482-11486, 1996), as applied to claim 43 above, and further in view of Zozulya et al. (Protein Eng., vol. 3, pp. 453-458, 1990).

A) Claim 44 is drawn to the proteorhodopsin gene of claim 43, wherein the host is a cell membrane preparation of a eukaryote.

B) Neither Kitajima et al. nor Shimono et al. teach the host being an artificial membrane system.

C) Zozulya et al. teach expression of bovine rhodopsin in cell-free translation system supplemented with artificial membranes, phosphatidylcholine liposomes (page 453, the last paragraph; page 454, first and second paragraphs). Zozulya et al. teach membranes prepared from eukaryotic microsomes of rat brain cortex and dog pancreas (page 454, third paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used eukaryotic membrane preparations of Zozulya et al. for placing a rhodopsin expression vector of Kitajima et al. and Shimono et al. The motivation to do so, as stated by Zozulya et al., would have been that "... The other obvious advantage of preparative cell-free expression system, as compared to the alternative ones, include: experimental simplicity and speed, the possibility of obtaining easily protein labeled with radioactive or modified amino acids, the possibility of inserting a membrane protein in a desired lipid environment co-translationally and, last but not least, comparatively low price of an experiment." (page 457, the last paragraph).

19. No claim are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (703) 306-5877. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

TS
August 13, 2003 TS

JEFFREY FREDMAN
PRIMARY EXAMINER